REMARKS/ARGUMENTS

Claim 1 is amended to incorporate the limitations of originally filed claims 8 and 10. Claim 10 is cancelled. No new matter is added. Nor do the above amendments raise new consideration or require new search. In fact, the above amendments are made to accommodate the Examiner's comments that unexpected results shown in the specification are not in commensurate with the scope of the claimed subject matter. Entry of the above amendments is respectfully requested. Upon entry of the above amendments, claims 1-9 are pending. Reconsideration of the present application is respectfully solicited.

Rejections under 35 U.S.C. §102(a)

Claims 1-10 stand rejected under 35 U.S.C. §102(a) as being anticipated by Lai et al. (Anti-Cancer Drugs, 2003, vol. 14, pages 825-828, accepted for publication on September 3, 2003). Applicants previously submitted a Rule 132 Declaration showing that Lai describes the inventors' own invention, not others'. However, in that Rule 132 Declaration, Applicants inadvertently omitted one of the co-inventors, Kuang-Chun Chiu's name. Applicants now submit a new Rule 132 Declaration executed by Kuang-Chun Chiu and some of the other co-inventors[1] showing that they are the true and only inventors of the present invention. Withdrawal of the rejections under 35 U.S.C. §102(a) is respectfully requested. Likewise, the potential rejection under 35 U.S.C. §102(f) as mentioned by the Examiner (the Office Action, page 3, last paragraph) also becomes moot in view of the new Rule 132 Declaration.

Rejections under 35 U.S.C. §103(a)

Claims 1-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ellison et al. (U.S. 2004/0115283) in view of Cheng et al. (J. Intern Med Taiwan 2003; 14:31-36), and Wu (U.S. Patent No. 6,127,688).

[1] One of the co-inventors, Chi-Liang Kan, is no longer employed with the Assignee and can not presently be located to execute the Declaration. Applicants believe that it is not necessary for each and every inventor to sign on the Declaration for the purpose to eliminate Lai et al. as an effective 102(a) reference. If the Examiner deems otherwise, he is respectfully invited to call the attorney of record to resolve this matter.

Claims 1-10 also stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ellison in view of Cheng, Wu, as applied above in connection with claim 9, and further in view of Medline abstract 95357499 and Medline abstract 84139233.

In Applicant's previous communication dated December 11, 2006, Applicants explained in detail that 1) there would be no motivation for a person of ordinary skill in the art to combine the teachings of the cited art; 2) a person of ordinary skill in the art would not have reasonable expectation of success by combining the cited art ; and 3) the "secondary considerations" such as "unexpected results" as shown in the originally filed specification further indicate hat the present invention is not obvious.

Nevertheless, in response, the Examiner still insists that the present invention is obvious over the cited art. It is believed that Applicant's previous explanation is sufficient in overcoming the Examiner's rejection. However, to expedite the prosecution, Applicants have now amended the claims in response to the Examiner's comments. Applicant preserve the right to pursue the originally claimed subject mater in a continuation or divisional application.

In response to Applicants' previous arguments regarding "unexpected results" shown in the originally filed specification (see e.g., page 8, line 1 to page 14, line 5, i.e., paragraphs 0020-0041, and Figs. 1-2), the Examiner states that such "unexpected results" are only limited to 0.01-0.5 mg/cm^2/day arsenic trioxide administered 1 hour prior to daily electron beam radiation treatment, at 5 days a week, 50 Gy in 25 fractions or 30 Gy in 10 fractions. (See the Office Action, page 15).

In response, Applicants now include the amount of arsenic composition, 0.01-0.5 mg/cm^2/day, and the total radiation range, 30-50Gy/5 days in claim 1. As to other limitations such as exact "1 hour" prior to daily electron beam radiation, 50 Gy in exactly "25 fractions", 30 Gy in exactly "10 fractions", only arsenic "trioxide", Applications believe that the Examiner's attribution of these particular limitations to the "unexpected results" are too limiting and not consistent with well-settled law.

For example, MPEP 6716.03(a) states,

> If a particular range is claimed, applicant does not need to show commercial success at every point in the range. "Where, as here, the claims are directed to a combination of ranges and procedures not shown by the prior art, and where substantial commercial success is achieved at an apparently typical point within those ranges, and the affidavits definitely indicate that operation throughout the claimed ranges approximates that at the particular points involved in the commercial operation, we think the evidence as to commercial success is persuasive."

(Emphasis supplied.)

MPEP 716.02(d) states,

> The nonobviousness of a broader claimed range can be supported by evidence based on unexpected results from testing a narrower range if one of ordinary skill in the art would be able to determine a trend in the exemplified data which would allow the artisan to reasonably extend the probative value thereof.

(Emphasis supplied.)

MPEP 2144.08 states,

> Additionally, the evidence must be reasonably commensurate in scope with the claimed invention.
>
> * * *
>
> When considering whether proffered evidence is commensurate in scope with the claimed invention, Office personnel should not require the applicant to show unexpected results over the entire range of properties possessed by a chemical compound or composition.
>
> * * *
>
> For example, a showing of unexpected results for a single member of a claimed subgenus, or a narrow portion of a claimed range would be sufficient to rebut a *prima facie* case of obviousness if a skilled artisan "could ascertain a trend in the exemplified data that would allow him to reasonably extend the probative value thereof."

Here, although the example in the specification only illustrates the effects of the use of arsenic trioxide administered 1 hour prior to daily electron beam radiation treatment, at 5 days a week, 50 Gy in 25 fractions or 30 Gy in 10 fractions, a person of ordinary skill in the art would readily extend the probable value thereof to the entire scope of claim 1. In addition, arsenic trioxide is specifically recited in claim 6, the beneficial effects of which are more specifically illustrated in the specification.

Therefore, the present claims 1-9 are not obvious over the cited art in view of the "unexpected results" as shown in the originally filed specification.

In addition, among other things, in Applicants' previous communication, Applicants explained that there is no reasonable expectation of success to modify Ellison based on the secondary references. Ellison provides a laundry list of various administration forms (see paragraph 0109-0128), a large number of different cancers (see paragraph 0051-0108 and 0129-0133), and various possible mechanism of actions (see paragraph 0031). It provides neither a specific example *(in vivo* or *in vitro*) nor other specific direction with respect to topical administration of arsenic composition. Nor does it provide any specific information related to treatment of cutaneous metastatic cancer.

Without any *in vivo* or in *vitro* test, it is difficult to predict whether a certain composition is effective and safe in treating a particular disease. See, e.g., MPEP 2164.03. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Here, as disclosed by Ellison, arsenic is well known to be both a poison and a carcinogenic agent (see paragraph 0022). Therefore, Applicants explained that there is no reasonable expectation of successes to modify Ellison based on other references, as suggested by the Examiner. In other words, even if a person of ordinary skill in the art would try to combine the teachings of Ellison with other references, as suggested by the Examiner, he or she would have to carry out undue experimentation to determine what specific disease can be treated by a specific arsenic composition in a specific manner of administration, etc. Therefore, the combination suggested by the Examiner is merely inadmissible "obvious to try" at most. See MPEP 2145X.B. The fact that Ellison limits its claims to treatment of only melanoma, despite the broad disclosure in the specification, seems to suggest that the specification does not fairly suggest or teach the treatment of all of the numerous cancerous diseases mentioned in the specification.

In response, the Examiner insists that mere disclosure of possible treatment of various cancers by various forms of arsenic compositions fairly suggests to a person of ordinary skill in the art that cutaneous metastatic cancer can be treated by administering to the cancer site with a topical arsenic-containing pharmaceutical composition followed by transcutaneous application of an electron beam (see the Office Action, pages 11-12). The Examiner states that the fact that Ellison only claims treatment of one specific cancer despite the very broad disclosure in the specification has no relevance to its teaching and suggestion to a person of ordinary skill in the art.

Based on Applicants' review of the file history of Ellison, the explanation and arguments of the Ellison inventors (see Exhibit 1, pages 4-8) clearly indicate that even the Ellison inventors themselves do not believe that a person of ordinary skill in the art would have reasonable expectation of success of treating a particular cancer with a particular administration form based on a broad teaching of various cancers and various forms. For example, at page 6 of Exhibit 1, Ellison's inventors state

> Those skilled in the art would have appreciated at the time of the invention that the efficacy of a particular anti-cancer agent against a specific type of cancer was not predictive of its efficacy against other types of cancers. It was understood that "[i]ncreasingly disease-specific therapies are being developed that will have optimum application for only one tumor type, although representing ineffective and toxic treatment and others."[2] Indeed, the therapeutic agents most commonly used to treat cancers at the time of the invention (and at present, as well) were effective only against specific types of cancers, and generally did not exhibit broad efficacy against numerous cancer types.[3] Accordingly, those skilled in the art would not have reasonably expected that arsenic trioxide could have been successfully used to treat melanoma in humans just because it have been reported to have efficacy against an unspecified type of skin cancer. Although those skilled in the art might arguably have considered trying to use arsenic trioxide to treat melanoma, the results of doing so could not have been predicted with a reasonable degree of certainty. Accordingly, those skilled in the art at the time of the invention would not have reasonably expected that arsenic trioxide could have been successfully used to treat melanoma in humans.

[2] Medical Oncology, Calabresi, P. et al., eds., 1985, Macmillan Publishing Company, page 257 (copy enclosed by the Ellison inventors as Exhibit B, which is not submitted here).
[3] *Id.* at 295-297.

In fact, even Examiner Pak himself admitted in another patent application related to arsenic composition (see Exhibit 2, first full paragraph, last six lines) that a mere broad disclosure of treatment of a laundry list of various cancers with various administration forms of an arsenic composition cannot fairly teach or suggest to a person of ordinary skill in the art treatment of each specific cancer with each specific administration form.

Accordingly, the Ellison inventors and Examiner Pak statements further indicate that there would be no reasonable expectation of success to modify Ellison based on other secondary references.

Withdrawal of the rejections under 35 U.S.C. § 103 (a) is respectfully requested.

Applicants believe that the present application is placed in condition of allowance. Early and favorable consideration is respectfully requested.

It is believed that no fees or charges are required at this time in connection with the present application. However, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
COHEN PONTANI LIEBERMAN & PAVANE LLP

By Kent H Cheng

Kent H. Cheng
Reg. No. 33,849
551 Fifth Avenue, Suite 1210
New York, New York 10176
(212) 687-2770

Dated: June 21, 2007